

REMARKS**The Pending Claims:**

Before entry of the amendments hereinabove, Claims 1-20 are pending in this application. Claims 1-20 are directed to a method of treating small intestinal bacterial overgrowth (SIBO) or a SIBO-caused condition in a human subject.

Applicants' Amendment

The amendment at page 1, lines 3-11, is to update the continuing data with respect to priority application U.S. Patent Application Serial No. 09/546,119, filed on April 10, 2000, which issued as U.S. Patent No. 6,558,708 on May 6, 2003.

The amendment at page 78, lines 27-30, is to correct obvious typographical errors.

Claims 1-20 are cancelled, without prejudice.

New Claims 46-85 are added.

Support for new Claim 46 is found, in the specification as originally filed, e.g., at page 1, line 24 through page 2, line 2; at page 28, lines 1-15; and in Claims 1 and 2, as originally filed.

Support for new Claim 47 is found, for example, in Claim 4, as originally filed.

Support for new Claim 48 is found, for example, in Claim 5, as originally filed.

Support for new Claim 49 is found, for example, in Claim 6, as originally filed.

Support for new Claim 50 is found, for example, in Claim 7, as originally filed.

Support for new Claim 51 is found, for example, in Claim 8, as originally filed.

Support for new Claim 52 is found, for example, in Claim 9, as originally filed.

Support for new Claim 53 is found, for example, in Claim 10, as originally filed.

Support for new Claim 54 is found, for example, in Claim 11, as originally filed.

Support for new Claim 55 is found, for example, in Claim 12, as originally filed.

Support for new Claim 56 is found, for example, in Claim 13, as originally filed.

Support for new Claim 57 is found, for example, in Claim 14, as originally filed.

Support for new Claim 58 is found, for example, in Claim 15, as originally filed.

Support for new Claim 59 is found, for example, in Claim 16, as originally filed.

Support for new Claim 60 is found, for example, in Claim 17, as originally filed.

Support for new Claim 61 is found, for example, in Claim 18, as originally filed.

Support for new Claim 62 is found, for example, in Claim 19, as originally filed.

Support for new Claim 63 is found, for example, in Claim 20, as originally filed.

Support for new Claim 64 is found, for example, in Claims 1, 2, 4, and 6, as originally filed.

Support for new Claim 65 is found, for example, in Claim 5, as originally filed.

Support for new Claim 66 is found, in the specification as originally filed, e.g., at page 1, line 24 through page 2, line 2; at page 28, lines 1-15; and in Claims 1 and 2, as originally filed.

Support for new Claim 67 is found, for example, in Claim 4, as originally filed.

Support for new Claim 68 is found, for example, in Claim 5, as originally filed.

Support for new Claim 69 is found, for example, in Claim 6, as originally filed.

Support for new Claim 70 is found, for example, in Claim 7, as originally filed.

Support for new Claim 71 is found, for example, in Claim 8, as originally filed.

Support for new Claim 72 is found, for example, in Claim 9, as originally filed.

Support for new Claim 73 is found, for example, in Claim 10, as originally filed.

Support for new Claim 74 is found, for example, in Claim 11, as originally filed.

Support for new Claim 75 is found, for example, in Claim 12, as originally filed.

Support for new Claim 76 is found, for example, in Claim 13, as originally filed.

Support for new Claim 77 is found, for example, in Claim 14, as originally filed.

Support for new Claim 78 is found, for example, in Claim 15, as originally filed.

Support for new Claim 79 is found, for example, in Claim 16, as originally filed.

Support for new Claim 80 is found, for example, in Claim 17, as originally filed.

Support for new Claim 81 is found, for example, in Claim 18, as originally filed.

Support for new Claim 82 is found, for example, in Claim 19, as originally filed.

Support for new Claim 83 is found, for example, in Claim 20, as originally filed.

Support for new Claim 84 is found, for example, in Claims 1, 2, 4, and 6, as originally filed.

Support for new Claim 85 is found, for example, in Claim 5, as originally filed.

The Office Action and Applicant's Response

The Examiner acknowledged Applicants' Response to Restriction, received 25 October 2002 (paper #6), and the cancellation of Claims 21-45, without prejudice, as being direct to non-elected subject matter.

The Examiner stated that the parent applications have been reviewed and asserted that they are not enabling for treatment of SIBO by depriving bacterial populations of nutrients or a single nutrient. Therefore, the Examiner stated that the effective filing date for Claims 1-20, which are drawn to said treatment, is the same as the actual filing date of the above-captioned application, i.e., April 17, 2001.

The Examiner stated that this application has been filed with informal drawings which are acceptable for examination purposes only and that formal drawings will be required when the application is allowed.

In response, Applicant herewith submits formal renderings of the figures.

The Examiner acknowledged Applicants' Information Disclosure Statement (mailed February 22, 2002), received 5 March 2002 (paper #4). However, the Examiner noted that the submitted Form PTO-1449 indicates a total of 18 pages, while pages 17 and 18 are merely copies of pages 15 and 16. Applicants regret this clerical error by which the Examiner received two copies of pages 17-18 of Form 1449 (listing references 162-177), two of which were erroneously hand-labeled as pages 15 and 16. The missing pages 15-16 (listing other references 137-161 and several patent references) were found in Applicants' records. On April 1, 2003, in a brief telephonic interview graciously granted to Applicant's undersigned attorney by Examiner Swartz, the Examiner clarified that a fresh copy of Applicant's entire IDS, including the previously missing pages 15-16, should be submitted (along with references 1-161; see below). Accordingly, Applicant herewith submits a fresh copy of Applicant's entire IDS, previously submitted, including the previously missing pages 15-16 of Form 1449.

Further the Examiner noted in the pending Office Action that page 1, paragraph 2, of Applicants' Transmittal of Information Disclosure Statement states that copies of references Nos. 137-161 and the patents on page 15 have been submitted with the IDS

form, however, no such references could be found in the application. In addition, the Examiner stated that in the files of the parent applications cited by Applicants, the Examiner could only find references 162-176. The Examiner stated that "the current examiner has made copies of the U.S. Patents listed on the IDS. The examiner expressed regrets for the inconvenience to the applicants, but if the rest of the nonpatent references listed as ref. Nos. 1-162 and 177 are to be considered, the examiner requests that copies of these references be submitted."

Although, Applicants' records indicate that references 137-161 were indeed mailed to the USPTO along with Applicants' Information Disclosure Statement (Paper No. 4), Applicant is pleased to submit herewith, for the Examiner's convenience, references 1-161 and the patent references listed on the true page 15 of Applicants' Information Disclosure Statement (Paper No. 4).

The Examiner acknowledged that the specification is "enabling for treatment of SIBO in irritable bowel syndrome patients with a predigested nutritional formula VIVONEX®."

However, none of original Claims 1-20 were allowed.

Claims 1-20 were rejected under **35 USC § 112, first paragraph**. The Examiner stated the following reasons:

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of SIBO in irritable bowel syndrome patients with a predigested nutritional formula VIVONEX® alone, does not reasonably provide enablement for treatment of SIBO or other SIBO caused conditions by deprivation of all/some nutrients or single nutrient nor of combination therapies with enzymes, absorption alterations, or any other therapies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention – method of treating SIBO or a SIBO caused condition in a human subject, said method comprising: 1) detecting SIBO, and if SIBO is present, 2) depriving the bacterial

population of nutrients sufficiently to inhibit the growth of said bacterial and thereby partially eradicating SIBO in said subject.

The state of the prior art indicated that SIBO is detectable in a variety of afflictions of mammals. Therapy includes surgery, diet changes (in dogs and cats), and/or antibiotic therapy to reduce the level of SIBO. Nutritional requirements of bacteria found in SIBO is well-known. However, the ability to alter the bacterial levels in SIBO through diet alone by depriving the bacteria of an essential nutrient or nutrients is not well known.

The amount of direction or guidance present – The instant specification provides any one example of the claimed nutrient deprivation method, i.e., example 11, which uses a commercially available composition, VIVONEX®, which comprises many predigested nutrients. All of the patients involved in the study are diagnosed with irritable bowel syndrome. No other patients with other diagnosis are included. There are no examples of single nutrient deprivation being successful for treating SIBO, nor is there guidance for determining which single nutrient would be successful. The example does not provide evidence that any conditions of the patients other than reduction in SIBO have been altered.

The quantity of experimentation necessary to fulfill the scope of the instant claims constitutes merely an invitation to experiment, without a reasonable expectation of success in determining what single nutrient treats SIBO.

The basis of rejection as to canceled Claims 1-20 is moot. As to new Claims 46-85, Applicants asserts that the specification does contain an enabling disclosure for the full scope of new Claims 46-85. The claimed invention is now more narrowly directed to a method of treating small intestinal bacterial overgrowth (SIBO) (e.g., new Claims 46-85) or SIBO-caused irritable bowel syndrome (e.g., new Claims 46-65), or a SIBO-associated condition in a human subject, said condition being selected from the group consisting of impaired mentation and impaired memory (e.g., new Claims 66-85). The teachings of the specification as originally filed, describe the underlying cause that links all of the disorders recited as SIBO-caused conditions. (See, e.g., specification, at page 27, line 26 through page 28, line 15; and Example 1-8, at page 60, line 17 through page 70, line 32; Claims 2-3 as originally filed).

The claimed method involves, *inter alia*, detecting in the subject, by suitable detection means, the presence or absence of SIBO in the subject, and if SIBO is detected “... depriving the population of nutrients sufficiently to at least partially eradicate SIBO in the subject.” (e.g., new Claims 46 and 66). The specification teaches that “[w]ith the growth of the bacteria constituting the SIBO condition thus

inhibited, SIBO is at least partially eradicated, as the subject's phase III interdigestive motility is better able to clear the small intestine of the overgrowth and sweep the bacteria into the colon for eventual elimination from the body." (Specification, at page 28, lines 6-10). In addition, Applicants' specification teaches that "the at least partial eradication of the SIBO condition also decreases the occurrence or magnitude of bacteria-related toxicity, sepsis (in more severe or advanced SIBO), and/or the subject's own immune responses, which are continually triggered by the presence of SIBO in non-immunocompromised subjects. The clinical symptoms of the subject associated with SIBO *or the SIBO-caused condition* are, consequently, ameliorated by the at least partial eradication of SIBO." (Specification, at page 28, lines 10-15).

Applicants agree with the Examiner that the nutritional requirements of bacteria found in SIBO are known in the prior art. Applicants also agree with the Examiner that the ability to alter the bacterial levels in SIBO through diet alone by depriving the bacteria of essential nutrients, in accordance with the claimed method, was not known, minus the disclosure of Applicants' specification. The specification as originally filed discloses that this can be accomplished by having the subject consume "a diet consisting essentially of nutrients that upon arrival in the upper gastrointestinal tract of the subject, are at least partially predigested." (E.g., new Claims 47-49, 64, 65, 67-69, 84, and 85; see, Specification, at page 40, lines 21-23). As an example of such a diet, the specification discloses "a comestible total enteral nutrition (TEN) formulation, which is also called an 'elemental diet.'" (Specification, at page 40, lines 26-28).

As the examiner noted, a working example of the claims is provided in Example 11, in which a particular TEN formulation (VIVONEX[®]) was used. The specification teaches (e.g., in Examples 4-6) that SIBO is an underlying cause of various conditions including IBS, impaired mentation and impaired memory. By way of confirmation of the teachings of the specification, Applicant also submits as **Exhibit A** the Declaration of Dr. Mark Pimentel, under 37 CFR Sec. 1.132, concerning two patients who suffered from SIBO-associated impairment of mentation and/or memory, and who were successfully treated in accordance with the claimed method (e.g., Claims 66 and 84; see **Exhibit A**, paragraphs 4, 4(a), and 4(b)). In light of the teachings of the specification

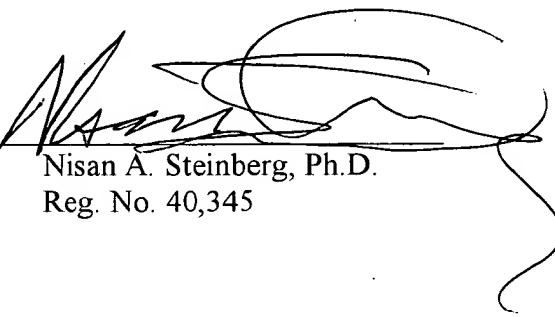
(further confirmed by Exhibit A) and the known nutritional requirements of bacteria found in SIBO, one skilled in the art would be able to make and use the full scope of the invention without undue experimentation by depriving the bacteria of known nutrients sufficient to at least partially eradicate SIBO.

CONCLUSION

In view of the above amendments and remarks, it is submitted that this application is now ready for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at (213) 896-6665.

Respectfully submitted,

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